



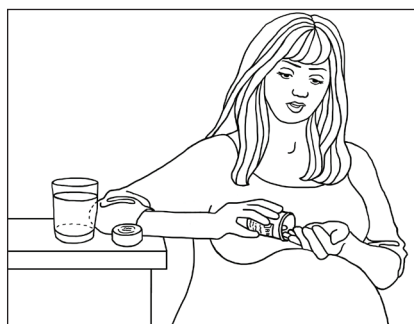
Early & Periodic Screening, Diagnosis & Treatment

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The Challenge of Detecting Prescription Opioid Abuse in Pregnancy

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The last 10-15 years in the United States has seen a dramatic shift in prescription opioid abuse.¹ Americans now consume 80% of the world opioid supply despite constituting only 4.6% of the world's population. Hydrocodone (Vicodin®, Lortab®, etc.) is now the leading prescription drug when all formulations containing this opioid are summed together. Oxycodone (OxyContin®, Percocet®, etc.) has steadily increased in prescriptions and is now in the top 20 most prescribed medications in the United States. Fentanyl and methadone prescriptions increased approximately fivefold and tenfold, respectively, in the 10 years from 1997-2007.



The increasing medical use of opioids has spawned greater availability of drugs that may get diverted and misused. Data from a variety of sources have documented increased overdose deaths, emergency room visits, and hospitalizations from prescription opioids. In 2007, opioids accounted for 11,500 deaths in the United States, more than heroin and cocaine combined.¹

Abuse of prescription opioids in pregnancy is a concerning problem.² Pregnant women may have access to medications from previous prescriptions, diversion from other people, or from prescriptions from non-obstetric providers. Intrauterine opioid exposure has been associated with intrauterine growth restriction, prematurity, and withdrawal symptoms. Neonatal abstinence syndrome in opioid-exposed infants can present with increased reflexes and muscle tone, abnormal sleeping and feeding patterns, diarrhea, vomiting, irritability, and high-pitched crying.

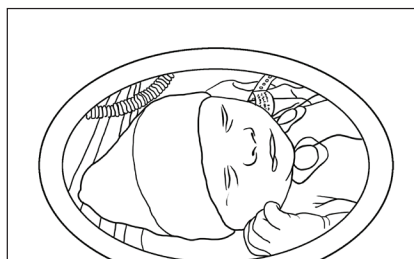
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Newborn Drug Screening

Due to the significant potential risk to the fetus and infant, timely detection of intrauterine drug exposure is paramount for peripartum and long-term clinical management.² Many institutions have developed internal policies that include newborn drug screening in cases identified as high risk for maternal drug abuse (e.g., prior history of maternal drug abuse, signs of drug withdrawal in the newborn). Drug testing may include mother or newborn or both.

The three main specimens used in newborn drug screening are urine (in mother and/or newborn), meconium, and umbilical cord.³ Urine drug testing has a brief window of detection for drugs of abuse. In addition, specimen collection can be challenging in newborns. In newborns, urine testing only captures drug use close to the time of delivery—up to a few days (especially for most opioids), or at most a week. Urine drug testing is unlikely to detect sporadic maternal drug abuse.

Meconium (infant's first stool) begins to form early in the second trimester and continues to accumulate throughout gestation. Meconium drug testing potentially detects maternal drug use in the second and third trimesters and has become the "gold standard" method for newborn drug screening.³ However, collection of meconium may be missed due to passage of meconium in utero prior to birth (especially in stressed fetuses), late passage



after hospital discharge, or inadvertent or intentional disposal of diapers containing meconium.

Drug abuse testing on umbilical cord tissue is relatively new but shows similar length of detection window compared to meconium.³ Umbilical cord tissue has the greatest ease of collection, with collection possible in every infant. Unlike urine or meconium, umbilical cord will not contain medications given to an infant. Umbilical cord may eventually supplant meconium as the specimen of choice.

Due to the potential clinical and social work consequences associated with a positive test result, it is imperative that confirmatory drug testing be used for definitive identification.²⁻³

Many clinical laboratories use an initial screening test (typically an immunoassay) for drug testing. Screening tests preliminarily identify the presence or absence of a class of drugs (e.g., opiates). However, there are a number of possible drugs that can cause opiates positive screen (e.g., codeine, morphine, heroin). Screening tests can also have false positives. Confirmatory testing typically uses mass spectrometry (often in techniques like gas chromatography, GC/MS, or liquid chromatography tandem mass spectrometry, LC/MS/MS) and can specifically identify exact compounds. For

example, an opiates positive specimen can be demonstrated by confirmatory testing to have codeine and morphine.

Detecting maternal prescription drug abuse by newborn drug screening

The single biggest challenge in identifying prescription drug abuse in pregnancy by drug testing is separating out misuse from other causes such as dietary poppy seeds, legitimate maternal prescriptions, or medications given to mother or infant in the peripartum period.²⁻³ Oxycodone, codeine, and morphine may be prescribed in pregnancy. Morphine may be administered to neonates prior to meconium collection. Poppy seeds also contain morphine and/or codeine. Further complicating the picture is that the metabolism (breakdown) of opiates in the body is complex (Figure 1 and Table 1). Certain compounds (e.g., hydromorphone) can be given as therapeutic agents, but are also known metabolites of other drugs in the pathway.

Interpretation of drug test results can be difficult. For example, detection of morphine in meconium or newborn urine could be from iatrogenic administration of morphine to mother or newborn, poppy seed ingestion by mother, or as a metabolite of codeine. Detection of oxycodone, codeine, or heroin (or its unique metabolite 6-monoacetylmorphine) in a sample is diagnostic of use of these compounds as they are not metabolites of any other opiates.

(continues on page 3)

Detecting Prescription Opioid Abuse in Pregnancy *(continued from page 2)*

These challenges underscore the importance of thorough maternal and newborn medication review. Failure on the part of the clinical team to recognize or collect such information could lead to inappropriate involvement by law enforcement or child protective services, as well as untold stress for the infant's family. In some cases, the drug testing results may be compelling but not clear-cut enough for definite conclusion of drug abuse by the mother.

Key points:

- Consider prescription opioid abuse in pregnancy.
- Recognize opioids commonly used in pregnancy and in the perinatal period for mother and infant.
- In cases of suspected prescription drug abuse in pregnancy, obtain a thorough maternal prescription drug history. This may necessitate obtaining medical records from other hospitals or pharmacies.
- Urine, meconium, and umbilical cord drug testing of newborns may pick up opioids from legitimate prescriptions and from poppy seeds in the diet.
- Confirmatory drug testing should be performed in cases of suspected maternal drug abuse in pregnancy. Screening drug tests on their own may have false positives or incomplete information.
- Utilize the metabolism pathways of opiates and benzodiazepines in interpreting drug abuse testing.

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Table 1
Common Opioids and its Major and Minor Metabolites

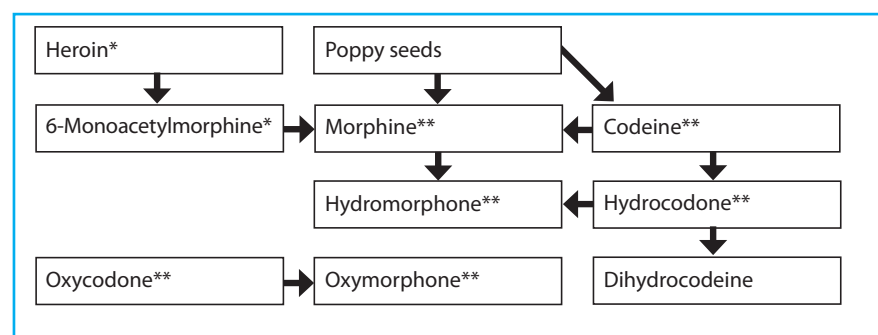
Drug	Major metabolite(s) detected by confirmatory drug testing	Minor metabolites that may be detected by confirmatory drug testing
Buprenorphine	Norbuprenorphine	
Codeine*	Morphine	Hydrocodone Hydromorphone
Fentanyl	Norfentanyl	
Heroin*,**	6-Monoacetylmorphine**	Morphine
Hydrocodone	Dihydrocodeine Hydromorphone	
Hydromorphone	None	
Methadone	EDDP	
Morphine	Hydromorphone	
Oxycodone*	Oxymorphone	

* Not metabolites of any opioids.

** Detection of either heroin or 6-monoacetylmorphine is diagnostic of heroin use.

* Heroin is illegal in the United States. Presence of 6-monoacetylmorphine is

Figure 1
Metabolism Pathways of Opiates



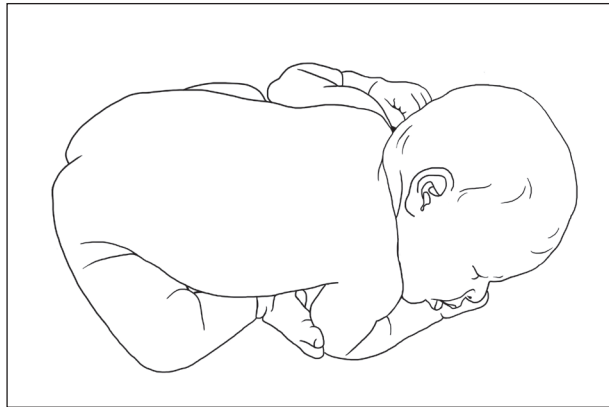
diagnostic of heroin use

** Drug may be legally prescribed in United States

Perinatal Illicit Substance Exposure and the Dilemma Related to Prescription Abuse

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Perinatal illicit drug use and in utero exposure to illicit drugs have been significant public health issues because of the associated medical, social, psychological, and legal consequences. It was reported that among pregnant women ages 15-44 years, 5% used illicit drugs in 2010-2011 in the United States. Other studies at urban hospitals have found that maternal illicit drug use during pregnancy ranges from 9-45% of all births.¹⁻² Because of maternal illicit drug use, 7-11% of infants born in the United States may be victimized by intrauterine drug exposure.² In Iowa, children exposed to illicit drugs either prenatally or postnatally compose the fastest growing population of children reported for abuse and neglect, quadrupling from 2000 to 2006 (2.4% in 2000, 9.4% in 2006). The current rates of approximately 5% do not reflect the actual proportion of drug exposed children in Iowa since Child Protection Services changed the criteria under which children are to be tested for illicit drugs since 2007.



newborn via meconium and/or umbilical cord tissue may be an option.

However, by the time the infant tests positive for illicit drugs, indicating in utero exposure, it is often too late to provide the mother and the newborn with the most

Illicit drug use has a wide spectrum of effects on fetuses and children such as low birth weight, intrauterine growth retardation, prematurity, microcephaly and some congenital malformations.² More importantly, infants born to mothers abusing drugs during pregnancy are often subjected to further drug exposure in their home environments, child abuse and neglect, and domestic violence.

The best approach to identify perinatal illicit drug exposure is to recognize the risk factors associated with it as early as possible during pregnancy via maternal interview and urine/hair toxicology testing of the mothers.² If the mother refuses to be tested, testing the

opportune interventional services. It was earlier reported that utilization of a structured screening protocol increased the number of neonatal testing for illicit drugs and positive testing rate. However, a study performed at the University of Iowa Hospitals and Clinics (UIHC) revealed that the adoption of a structured protocol did not ensure that the staff would necessarily utilize it unless a structured, staff training program on the proper use of the protocol is also implemented.³ As a result of these observations, the UIHC Child Protection Program collaborated with the Iowa Perinatal Care Program and developed a new structured protocol that was adopted by multiple birthing hospitals as well as the UIHC in 2007.

(continues on page 5)

Risk Assessment Tool

(See Insert, page 6)

The use of this protocol and risk assessment tool led to very positive results at the UIHC.

1 The risk assessment tool was made part of the online documentation system at the UIHC, thus, every pregnant or delivering woman and newborn was screened routinely. Associated with the new structured protocol, the leaders of the program developed a training module to educate the staff on the importance of complying with the protocol and how to use it. Staff from the following departments and units were trained to utilize the training modules and the new protocol, and to become trainers for their unit staff: Prenatal Clinic, Labor & Delivery Unit, Mother & Baby Unit, Neonatal Intensive Care Unit, Department of Psychiatry, Chemical Dependency Unit, and Department of Social Services. The trainers trained all relevant unit staff under their supervision.

This training module consisted of three separate, unit-specific, in-service training video clips. One video was presented to staff involved in obstetrical and prenatal care in the Prenatal Clinic; another to staff in

the Labor and Delivery Unit; and a third to staff in the Mother/Baby and Neonatal Intensive Care Units. After watching the training videos all staff had to complete a posttest composed of 10 questions. Staff needed to correctly answer eight of the 10 questions in order to receive their certificate of completion of this mandatory training.

Documentation of posttest results was kept by the leading author to ensure all staff completed the necessary training requirements. The training of all staff in the above listed units was completed between July 1, 2007 and December 31, 2008.

2 The charts of dyads consisting of mothers and their newborn offspring receiving pregnancy, delivery, and/or newborn services at the UIHC were reviewed. Data was collected in two groups selected on the following basis:

a Pre-training control group (Pre-TG): All mother-infant dyads (n=1,186) admitted to the UIHC through Obstetrics and Prenatal Clinic, Labor and Delivery Unit, Mother/Baby Unit, or the Neonatal Intensive Care Unit between January 1, 2006 and December 31, 2006 constituted the control group for this study. The data collection on this group was performed

as part of a previous descriptive study by review of handwritten charts and an early version of UIHC online charting system.³

b Post-training intervention group (Post-TG): All mother-infant dyads (n=1,855) admitted to the UIHC through Obstetrics and Prenatal Clinic, Labor and Delivery Unit, Mother/Baby Unit, or the Neonatal Intensive Care Unit between January 1, 2009 and December 31, 2009 constituted the study group. Data collection on this group was completed by review of the online UIHC charting system that was developed as a part of the intervention.

3 As a result of the intervention, significant positive developments occurred in multiple areas related to perinatal illicit drug use and exposure. It is hoped that every hospital providing prenatal care, labor and delivery, and newborn care services would adopt this protocol as soon as possible coupled with developing a staff training program to get the best benefits out of this program. (See Table 1, page 7)



(continues on page 7)

UIHC Perinatal Illicit Drug/Exposure RISK ASSESSMENT TOOL



Obstetrics Clinic and Labor and Delivery Unit

► Risk Factors Related to Current Pregnancy

Maternal urine drug screen positive Yes... No
 Maternal report of illicit drug use Yes... No
 No prenatal care or late prenatal care
 (> 16 weeks gestation) Yes... No
 Unexplained poor prenatal care
 (≤ 4 prenatal visits) Yes... No
 Unexplained abruptio placenta Yes... No
 Unexplained premature delivery Yes... No
 Unanticipated out-of-hospital delivery Yes... No
 Unexplained discrepancy between delivery/
 prenatal care facilities (hospital hopping) .. Yes... No
 Unexplained presentation at hospital in
 second stage of labor Yes... No
 Unexplained precipitous labor (<3 hours) Yes... No
 Unexplained episode of acute hypertension
 (≥140/90 mmHg) Yes... No
 Unexplained seizures, stroke, or myocardial
 infarction Yes... No
 Tobacco or alcohol use Yes... No
 Physical attributes suggesting illicit drug use
 such as IV track marks, visible tooth decay,
 sores on face, arms, or legs Yes... No
 Altered mental status suggesting influence/
 withdrawal from illicit drugs Yes... No
 Unexplained stillbirth Yes... No

► Risk Factors Related to Maternal Medical History

Unexplained Hepatitis B or C, syphilis, or HIV within the last
 3 years Yes... No
 Untreated maternal depression or major psychiatric illness
 within the last 3 years Yes... No
 Ever used illegal drugs during any pregnancy Yes... No
 Ever delivered an infant who tested positive for illicit drugs... Yes... No

► Risk Factors Related to Maternal/Family Social History

History of illicit drug use by mother or partner within the last
 3 years Yes... No
 History of illicit drug rehabilitation by mother or partner
 within the last 3 years Yes... No
 History of domestic violence by partner within the last
 3 years Yes... No
 History of child abuse, neglect, or court ordered placement
 of children outside of home of this patient Yes... No

► If any of these questions are answered with YES, the following should be done:

- ☐ Request informed consent from the mother to order urine screening for illicit drugs
- ☐ Contact the unit social worker to initiate detailed psychosocial assessment
- ☐ Request Chemical Dependency Services consult if the social worker and the physician believe it is warranted
- ☐ Request Psychiatry consult if mental health problems recognized
- ☐ Communicate the risk status with Newborn Nursery or NICU staff verbally (for L&D staff)
- ☐ Attach copy of this form to Labor and Delivery Form and send to the Newborn Nursery or NICU along with the baby

Newborn Nursery/NICU Bays 1-4

► Risk Factors Related to Newborn Assessment

Maternal risk factor(s) present Yes... No
 Mother was tested during this pregnancy
 or labor for illicit drugs Yes... No
 Mother tested positive for illicit drugs
 during this pregnancy Yes... No
 Gestation ≤37 weeks from unexplained
 preterm delivery Yes... No
 Unexplained birth weight less than 10th
 percentile for gestational age Yes... No
 Unexplained head circumference less than
 10th percentile for gestational age Yes... No
 Unexplained seizures, stroke, or brain infarction Yes... No
 Unexplained symptoms that may suggest drug withdrawal/
 intoxication: high-pitched cry, irritability, hypertonia,
 lethargy, disorganized sleep, sneezing, hiccoughs,
 drooling, diarrhea, feeding problems, or
 respiratory distress Yes... No
 Unexplained congenital malformations involving
 genitourinary tract, abdominal wall, or
 gastrointestinal systems Yes... No

► **Staff should order meconium and urine screening tests for illicit drugs if the answer is Yes to one or more questions under the Maternal or Infant Risk Assessment Tool.**

Table 1: Comparison of Pre-TG (2006) and Post-TG (2009) dyads' variables (n,(%))

	Pre-TG	Post-TG	P value
Maternal drug testing performed	73 (6.2)	300 (16.1)	<0.001
Maternal positive drug testing	15 (1.3)	69 (3.7)	<0.001
Social worker involved in case	87 (7.3)	610 (32.8)	<0.001
Maternal referral for substance abuse evaluation	8 (0.7)	39 (2.1)	0.002
Maternal referral for substance abuse treatment	8 (0.8)	13 (0.7)	0.760
Maternal referral to mental health evaluation	89 (7.6)	259 (19.1)	<0.001
Maternal mental health treatment	87 (7.4)	310 (23.8)	<0.001
Infant drug test performed	144 (12.3)	554 (30.1)	<0.001
Positive infant drug test	11 (0.9)	127 (6.9)	<0.001
Missed opportunities for testing infants	248 (20.9)	10 (0.6)	<0.001
<p><i>Pre-TG: Pre-training group Post-TG: Post-training group</i></p> <p><i>NA: Not applicable since substance abuse treatment took place outside of the study institution for those who were referred for treatment.</i></p>			

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